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CASE REPORT

Strabismus surgery for diplopia in chronic progressive external ophthalmoplegia

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Abstract
Background To report midterm outcomes of strabismus strategy for management of diplopia in chronic progressive external ophthalmoplegia and specific surgical planning rationale.
Design Retrospective interventional case series.
Results Two patients, a 26-year-old male and a 36-year-old female, diagnosed with chronic progressive external ophthalmoplegia presented with blepharoptosis and intermittent diplopia. Ocular motility examination was significant for bilateral profound impairment of adduction with relative preservation of abduction, infraduction and elevation. Control of intermittent exotropia gradually worsened over 3 and 1.5 years of follow-up, respectively, in the presence of documented stability of the angle of exodeviation. Strabismus surgery involving modest amounts of bilateral medial rectus resection and lateral rectus recessions was undertaken. Surgical intervention was successful in controlling alignment in primary position and alleviating diplopia and asthenopia after 9 and 8 years of follow-up time, respectively, despite slow progression of ophthalmoplegia.
Conclusion Bilateral selective impairment of adduction and intermittent exotropia may be the presenting ocular motility disturbance in chronic progressive external ophthalmoplegia. Properly designed strabismus surgery may provide sustainable, in the midterm, control of alignment and symptomatic relief in selected patients with CPEO.

Keywords Chronic progressive external ophthalmoplegia · Strabismus surgery · Diplopia management in CPEO

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Introduction

Chronic progressive external ophthalmoplegia (CPEO) is characterized by slowly progressive blepharoptosis and bilateral impairment of ocular motility attributed to a mitochondrial myopathy [1, 2]. The hallmark finding is the presence of "ragged red fibers" on histological examination of skeletal muscle biopsy specimens; they represent accumulation of structurally abnormal mitochondria [3]. Deletions of various lengths in mitochondrial DNA result in defective

translation of protein subunits of enzymes necessary for oxidative phosphorylation [4]. The resultant deficits in mitochondrial function are most prominent in highly oxidative tissues such as muscle, brain and heart.

Extraocular muscles, due to their high mitochondrial volume fraction, in comparison with other skeletal muscles are preferentially affected. The involvement of extraocular muscles is usually symmetric and slowly progressive; it is therefore suggested that patients may not commonly report diplopia [5, 6]. We report on two patients who presented with diplopia and ocular motility impairment in the context of chronic progressive external ophthalmoplegia who benefitted from a sustained outcome of strabismus surgery. Institutional Review Board (IRB) approval from the Athens General Hospital "G. Gennimatas" was obtained for reporting data from the patients' charts.

Report of cases

Case 1

A 26-year-old white man presented complaining of intermittent diplopia and asthenopia of 2-year duration. Ophthalmic history was significant for the development of bilateral blepharoptosis at the age of 13. He had been submitted to bilateral frontalis sling operations with a successful postoperative result. He already carried the diagnosis of mitochondrial myopathy based on deltoid muscle biopsy positive for ragged red fiber. His prior workup included a negative edrophonium test for blepharoptosis. Electrocardiography was negative for Kearns–Sayre syndrome-related conduction disturbances.

Best corrected visual acuity was 20/20 in either eye. The prism and alternate cover test disclosed 35 prism diopters (PD) of intermittent exotropia at distance and 40 PD at near.

Assessment of ocular motility was significant for profound limitation of adduction in both eyes. Based on a scale of − 4 (maximum underaction) to + 4 (maximum overaction), he demonstrated − 3.5 in adduction in both eyes with clinically preserved elevation, depression and abduction (Fig. 1a). A fine jerk nystagmoid movement was noted in the abducting eye. Ten prism diopters of base-in prisms were prescribed and were helpful in controlling asthenopic symptoms.

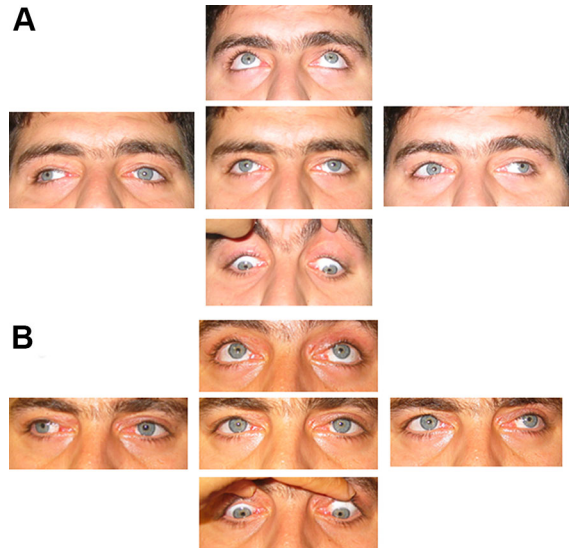

Fig. 1 Case 1, ocular alignment in the five cardinal positions of gaze in the setting of intermittent exotropia. Preoperatively (**A**) a pronounced impairment of adduction with relative preservation of elevation, depression and abduction is noted in the 28-year-old patient with chronic progressive external ophthalmoplegia. In the pictures taken 3 years after strabismus surgery (**B**) exodeviation is controlled in primary position yet a mild impairment of abduction and elevation is noted in both eyes

The angle of deviation remained stable throughout 3 years of follow-up time. Asthenopia, though, worsened significantly overtime. A deterioration in the control of intermittent exotropia was confirmed by orthoptic examination. He was unable to fuse the Worth Four Dot test at distance. Prism management was no longer sufficient to relieve the patient's symptoms.

At the age of 29, the patient was submitted to bilateral lateral rectus recessions of 4.00 mm and bilateral medial rectus resections of 4.00 mm under general anesthesia. The administration of muscle relaxants was kept to minimal doses. Intraoperative forced duction testing was mildly positive in adduction.

Alternate prism and cover test at 6 weeks postoperatively showed 8 PD of exophoria at distance and 12 PD at near. Asthenopic symptoms were relieved, and the patient was able to sustain reading which allowed him to resume his studies in graduate school. The adduction deficit persisted postoperatively (Fig. 1b).

Upon his last examination, 9 years after the operation, he measured 5 PD of intermittent exotropia at distance and 10 PD at near. He could fuse the Worth Four Dot test at distance. Ophthalmoplegia has progressed to a mild limitation of abduction and elevation in both eyes.

Case 2

A 36-year-old woman presented with a 5-year history of intermittent binocular diplopia, which tended to become constant for the last 2 years. She reported blepharoptosis since age 13 and had undergone eyelid surgery for ptosis in the left eye. She was diagnosed with mitochondrial myopathy at the age of 35, based on histological findings of ragged red fibers on skeletal (deltoid) muscle biopsy. She had a negative workup for myasthenia gravis (negative tests for acetylcholine receptor antibodies, muscle specific kinase antibodies and single-fiber electromyograph) and negative thyroid function test. Magnetic resonance imaging (MRI) of the brain was unremarkable; an orbit MRI indicated thinning of the extraocular muscles. Consultation by a cardiologist did not indicate conduction arrhythmias.

Best corrected visual acuity was 20/20 in either eye. Based on a scale of − 4 to + 4, she had − 3.5 adduction of the right, − 3 in adduction of the left eye, and − 2 in elevation and − 1 depression of either eye (Fig. 2a). The cover test showed poorly controlled intermittent exotropia, with 25 PD right exotropia in primary gaze, and 30 PD exotropia at near. A diplopic response was noted on the Worth Four Dot test.

She was followed for 15 months; diplopia persisted and cover test measurements had remained stable in primary position. In December 2009, she underwent strabismus surgery consisting of right medial rectus resection of 4.00 mm, right lateral rectus recession of 5.00 mm and left lateral rectus recession of 5.50 mm. Intraoperative forced duction testing was mildly positive in adduction and elevation. On the first postoperative day, she was overcorrected; by alternate prism and cover test, she measured 20 PD of left esotropia which had decreased to 10 PD by 15 days postoperatively.

By 3 months postoperatively, she was orthophoric in primary position, 1–2 PD esophoric in left gaze and downgaze. At the last examination, 8 years postoperatively, ocular motility impairment had slightly progressed to mild limitation of abduction in both eyes

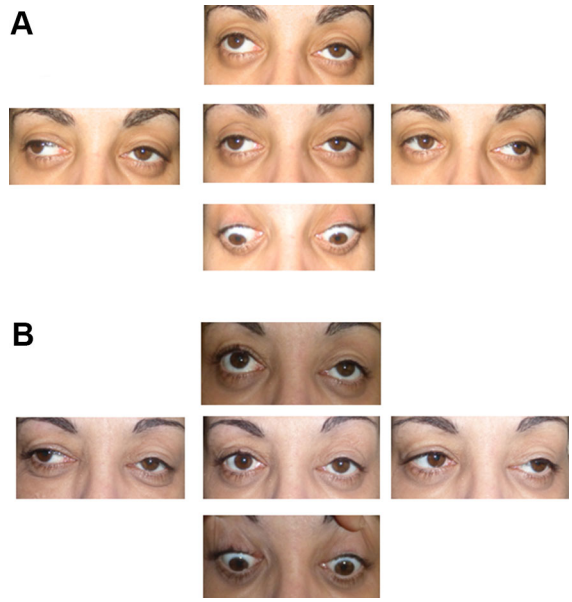

Fig. 2 Case 2, ocular alignment in the five cardinal positions of gaze preoperatively (**A**) and postoperatively (**B**). Orthotropia was achieved postoperatively in primary position and a slow progression in ophthalmoplegia was noted 8 years postoperatively

(Fig. 2b).The patient was orthophoric at distance and measured 3 PD esophoria in left gaze. She fused the Worth Four Dot test at distance and demonstrated 40 s/arc stereopsis on Titmus test.

Discussion

Exotropia is the most common type of strabismus deviation associated with CPEO. Up to ninety percent of patients [2] present with exodeviations.

Marked symmetry of involvement between paired extraocular muscles is reported as characteristic for patients with CPEO [2]. In their detailed study on ocular motility findings in CPEO, Richardson et al. [2] reported an average excursion of 22° (range: 17–27) for the medial rectus muscles with a symmetry of movement for the medial rectus muscle between 0° and 5° in 70% of cases. The mean exodeviation in that study [2] was 20 PD; Tinley et al. [7] reported a mean of 47 PD exodeviation in their series. The ocular motility pattern encountered in the two patients was characterized by a pronounced, fairly symmetric selective limitation of adduction with minimal involvement of other ocular movements which has

not been highlighted as a common feature of CPEO in the accessible to us literature.

Strabismus surgery, although not the first-line of management, may be considered in CPEO. Some authors [8] have advocated caution in regard to surgery for strabismus associated with CPEO, because the alignment is prone to change due to the progressive nature of the disease and there are poor chances to obtain satisfactory binocular vision in these patients [9].

A limited number of small case series [10–12] have addressed surgical options for strabismus in CPEO in the literature so far. In a series of 28 patients with strabismus in the context of CPEO [7], eight patients underwent strabismus surgery, constituting the largest strabismus interventional series in CPEO published so far. The authors advocate the use of maximal recessions of rectus muscles due to the propensity for undercorrections.

Earlier reports [1, 10] supported the viewpoint that resections alone should be considered as primary procedures in CPEO given the fact that recessions alone may result in undercorrection. Sorkin et al. [12] based on intraoperative findings of marked reduction in extraocular muscle tone, which rendered "taking up the slack" during postoperative adjustment of recessed muscles impossible, suggested that rectus muscle resections are far more effective than recessions for correcting strabismus associated with chronic progressive external ophthalmoplegia.

We opted for a combination of modest amounts of recession and resection of three or four horizontal muscles to address an exodeviation in the moderate preoperative angle range; we thus avoided excessive weakening of already weak muscles on the one hand, and at the same time excessive amounts of resections of tentatively tight muscles against which weak and/or recessed muscles will have to counteract. We did not use adjustable sutures in these two patients, mostly based on preoperative assessment of cooperativeness (Q-tip tolerance test) that was estimated to be poor.

For patients with CPEO, exceeding the amount of surgical corrections that has been recommended in standard strabismus tables has been advocated by previous authors [7, 11]. Our data show a dose–effect ratio of 1.6 PD/mm of muscle recessed or resected in the former and 1.7 PD/mm in the latter patient, corresponding to a relatively low effectiveness of the procedure. These data confirm the necessity to exceed the amount of surgery regularly planned for the same amount of preoperative exodeviation in a nonmyopathic patient.

Various abnormalities in extraocular muscle properties may be encountered intraoperatively in CPEO, ranging from atrophic and flaccid muscles [12], making recession difficult, to fibrotic, inelastic muscles [7].

Except for a mildly positive intraoperative forced duction test in adduction, we did not encounter overt abnormalities in the horizontal recti muscles we did operate on. It is evident that the surgical plan, when dealing with surgical management of strabismus in CPEO needs to be individualized, guided by: (1) forced duction testing; if positive, recessions of appropriate muscles should be an integral part of the procedure, (2) intraoperative findings regarding elasticity and tightness of rectus muscles; if flaccid, the recessions should be anticipated to be less effective than expected. Extremely tight muscles need caution in manipulation [7].

Patients with strabismus in the context of CPEO reportedly have poor motor fusion, and it has been stated that diplopia often persists postoperatively, despite a small deviation [7, 11]. Surgery for our two patients was successful in addressing their chief complaint of diplopia and asthenopia, a benefit sustained for 9 and 8 years of follow-up time, respectively, despite slow progression of ophthalmoplegia.

We suggest that stable midterm postoperative results in these two patients may be associated with the fact that we intervened at a relatively early stage in the myopathic process, when motor fusion reserves had not decompensated, as evidenced by the intermittent character of the deviation and the relative preservation of vertical eye movements.

We speculate that our strategy of small amounts of recession-resection offers the additional advantage of inducing minimal secondary muscle changes, in contrast to large resections [10, 12] or large recessions [11] alone. This may prove beneficial to these patients in the long term, given the increased probability for another operation within the lifespan of a patient diagnosed with a progressive myopathic process.

Of note to the clinician is the increased sensitivity of patients with CPEO to anesthetic induction agents and nondepolarizing muscle relaxants [6].The anesthesiologist should consider a drastic decrease in

administered doses in order to avoid being faced with prolonged awakening.

Selected patients with CPEO may benefit from properly designed strabismus surgery, even at an early stage of ocular motility impairment with sustainable, in the midterm, benefits in binocularity, relief from diplopia in primary position and improvement in the quality of life.

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